BEDSIDE MEDICINE FOR BEDSIDE DOCTORS

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ROUTINE PRECAUTIONS IN SEROTHERAPY

ETIOLOGY AND PATHOLOGY OF SERUM SICKNESS

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Serum sickness is such a common sequel to the use of antisera of all sorts that a discussion of the subject, even from the viewpoint of theoretical immunology, is germane to the daily experience of the practicing physician.

Serum disease may be divided into two general types. First, the simple exanthem of protean character (urticarial, morbilliform, or scarlatinal), accompanied by fever, painful swollen joints, lymphadenitis, and a moderate degree of albuminuria with, less frequently, some degree of polyneuritis, myalgia, peripheral nerve paralysis and persistent arthritis. This, the common form of the disease, occurs six to fourteen days after the administration of serum, although it may very rarely follow immediately upon serum injection. The symptoms may recur without further injections at intervals of two to five days, and there are recorded as many as four separate eruptions after a single injection.

As to incidence, it may be categorically stated that the larger the amount given, and the more rapid the absorption into the blood stream, the more frequently does the disease appear. The data given below are tabulated from several sources and show the tremendous variation in incidence following single injections of varying quantities of antitoxic sera.

Statistically, the practitioner may assume that following the administration of moderate amounts of purified and concentrated serum given intramuscularly, one in five patients will manifest the disease. This compares most favorably with the earlier figures of 50 to 90 per cent incidence noted with whole horse serum before the purification technique had been developed.

The second and more malignant form of serum sickness fortunately occurs infrequently, and is characterized by acute shock with anxiety, pallor, dyspnea, rigors, and a rapid and feeble pulse; and is sometimes accompanied by vomiting, diarrhea, and a rapidly progressive edema of the face, pharyngeal tissues and lung. The outcome is occasionally fatal.

TABLE 1.—*Incidence of Serum Sickness as Related to Amounts Administered*

Volume of Serum	Percentage Showing Reaction
1-10 ml.	10
10-20 ml.	30
20-30 ml.	30
30-50 ml.	42
50-100 ml.	55
Over 100 ml.	70

This more violent manifestation of serum sickness has its onset immediately following intravenous or intraspinal injections of sera, although the literature contains accounts of its occurrence even after subcutaneous administration. Rarely may the onset be delayed until the appearance of the exanthem.

The physician may expect an incidence of one case of the fatal acute form per one hundred thousand serum injections. The immediate or delayed local reaction not infrequently takes the form of an extensive necrosis at the site of injection, corresponding closely to the Arthus phenomenon seen in experimental animals.

In considering the etiology of serum sickness one might be tempted, as a first approximation, to call the syndrome the exact analogue of anaphylaxis in experimental animals; but such is not altogether the case. In the first place, the symptoms most often follow a first injection of serum with an interval varying from a matter of minutes to some ten days. There is, thus, no sensitizing dose as in animals. Again, one would postulate an immediate anaphylactic response upon successive injections of serum if we assume the mechanism to be a truly anaphylactic one. All the essentials for the reaction are present, that is, there is precipitin free in the blood stream, and corresponding antigen is introduced. Yet immediate symptoms are very rare and some data indicate that serum sickness after a second injection of serum occurs less frequently than after a first. It is obvious, therefore, that certain objections must be overcome before the clinical and the experimental pictures may be considered analogous.

It may be well to summarize available data before attempting to depict the mechanism involved in the production of the clinical syndrome.

(*a*) Symptoms are due to the foreign serum *per se* and not to the antibody content; for the disease may be produced with sterile normal horse serum. Further, immunization with antigens resulting in the production of antibodies in the blood stream does not increase the percentage incidence of serum sickness.

(*b*) The symptoms are more apt to be produced by the serum of certain horses than by identically prepared serum from other horses. The variation in incidence with serum from different horses

varies from 20 to 90 per cent. This cannot be entirely controlled by pooling sera, for with such preparations the incidence will vary from 30 to 60 per cent.

(*c*) Concentrated serum is not so apt to produce serum sickness as whole serum, primarily because such sera may be given in smaller amounts and the total dose of foreign protein is consequently lessened. Also purified sera are antigenically less complex, since they consist of the pseudoglobulin fraction alone with the euglobulins and albumins removed.

(*d*) Horse serum fibrinogen is not the responsible etiologic agent.

(*e*) Active sensitization against horse serum can be produced in humans, as indicated by skin tests conducted before and after immunization with toxin-antitoxin.

With the clinical picture of serum disease in mind, and also considering the data mentioned above, we cannot state that the syndrome is explicable upon the same relatively simple basis as anaphylaxis in experimental animals. It is possible that the exanthem and accompanying clinical phenomena represent the typical human anaphylactic response which, for its development, requires well-defined quantitative and localizing conditions; as, for example, fixation of precipitin in epidermal cells. In addition man may possess, as do certain other animals, an inherent refractory state to the development of anaphylaxis, and it is likely that sensitization follows upon contact with horse proteins through channels other than direct injection. It would be said, then, that in the common form of the disease the foreign protein constitutes an antigen, and causes the production of antibodies while itself remaining in considerable concentration in the blood stream. When the antibodies have reached a certain critical concentration, the typical reaction occurs and symptoms follow. Upon these assumptions, which rest for the most part upon experimental evidence, it would be possible to explain the clinical manifestations and variations of serum disease as merely special cases of an antigen antibody anaphylactic reaction.

The pathologic changes in serum disease may be briefly disposed of. The swollen joints are usually not red nor do they show any increased temperature. The joints seldom contain free fluid and the swelling may be explained on the basis of periarticular edema. The fluid found in the joint cavity in the exceptional case shows the cytological findings of an acute arthritis, and in such fluid horse serum has been demonstrated. The local changes may then be due to synovial irritation from the localized foreign protein.

The regional lymph nodes, especially those nearest the site of injection, usually become swollen and tender quite early in the course of the disease, and similarly they regress early. This again is largely an edematous swelling which practically never progresses to suppuration. Exceptionally the spleen may become palpable.

The face, more particularly the eyelids and, in addition, the dependent parts of the body, often show a well-defined edema which is apparently not of renal origin but rather due to local changes in vascular permeability. It is not unusual to find signs of transitory renal irritation which for the most part, appear after the edema is established. During the first few hours of serum sickness there is apt to be a slight leukocytosis, with a moderate increase in the lymphocytes. As the syndrome progresses, the picture changes to a leukopenia, frequently accompanied by a mild eosinophilia.

In summarizing, one would conclude that serum disease is exceedingly protean in its manifestations, that its incidence and severity are related to the amounts of serum injected, the route of injection and the antigenic complexity of the serum used; and finally, that the syndrome is probably explicable as a special case of an anaphylactic reaction.

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TREATMENT AND PRECAUTIONS IN ADMINISTRATION OF SERUM

EDWARD B. SHAW, M. D. (384 Post Street, San Francisco). — The therapeutic use of serum in human beings is frequently followed at varying intervals by reactions which are, in general, no more than annoying, but are occasionally so distressing or dangerous as to necessitate weighing the benefits of serum therapy against these possible adverse effects. Such reactions include those due to nonspecific protein effect, and those in which specific hypersensitiveness is concerned.

Nonspecific Reactions. — The injection, especially intravenously, of any protein or protein-like material, serum, vaccines, pollen solutions, proteose, etc., is frequently followed in a few minutes by a reaction of varying severity. Adults are commonly more affected than children. There is commonly a rise of pulse and temperature which is sometimes to extreme heights, accompanied by chills, convulsions, nausea, vomiting, and prostration. The patient is frequently wretchedly uncomfortable, but there is usually little cause for concern unless the patient's antecedent condition is of such gravity as to impair his ability to withstand such a reaction.

Care in preparation of serum helps in the prevention of these occurrences. The blood of certain horses is more productive of reactions than others, and these should not be used as serum producers. Proper ageing, concentration, and clarification of serum are important.

Intravenous therapy is more dangerous and should be reserved for more serious conditions. When serum is thus employed it must be perfectly clear, should be warmed to body temperature and given very slowly. The coincident injection of dextrose solution has a protective effect.

The chills, hyperpyrexia, and general discomfort are treated symptomatically. Ice caps, cool baths, and continuous, cool colonic saline flushes help reduce the fever. Barbiturates, codein, or morphin are required for sedation. Epinephrin has no place in the treatment of this condition:

it does not serve to ameliorate the symptoms, and it adds to the tachycardia and general discomfort of the patient.

Specific Reactions. — A second group of reactions is due to specific horse serum hypersensitiveness. These reactions may be further divided into two groups—immediate reactions and delayed reactions.

Immediate reactions promptly follow serum administration. They are most violent after intravenous injection; but symptoms may appear after the introduction of a very small amount of serum, and fatal results have followed even subcutaneous reactions. Symptoms closely resemble anaphylactic shock in the guinea-pig; the patient is apprehensive, the skin tingles, urticaria may appear, there is increasing dyspnea, stridor, cyanosis, and finally death results from respiratory failure; or recovery may slowly occur with or without treatment. The picture is so similar to that of anaphylaxis that sometimes the phenomena are assumed to be identical. There is little doubt that the processes are not identical, but certain points of resemblance as well as certain differences are noteworthy clinically.

These reactions resemble anaphylaxis in their symptomatology, in the fact that other evidences of the patient's horse serum hypersensitiveness can often be discovered, and also in the fact that epinephrin is almost specific in the control of symptoms.

The differences between the experimental and clinical phenomena must be no less carefully noted:

1. Patients who develop anaphylaxis-like shock are frequently those with no history of previous serum injection. Unlike the experimental animal which is sensitized by the injection of a small amount of the specific protein at an interval prior to the shocking injection, the mechanism of sensitization in human beings often cannot be determined, and apparently in some cases is a constitutional factor which is unaffected by the patient's environment. Doubtless sensitization occurs in other ways than by injection, but some individuals are profoundly horse serum sensitive without any known previous contact with horse proteins.

It has been denied by some that human beings can ever be artificially sensitized to foreign protein, and it is certain that some individuals fail to exhibit any adverse reaction from several injections of serum at varying intervals. It is hardly less certain that other patients are rendered mildly, or sometimes profoundly, sensitive to horse serum after receiving one or more injections, and thereafter react more or less violently to subsequent injections. Single injections are less apt to sensitize than repeated ones, and such a procedure as the administration of three or four doses of T. A. T., which contains minute amounts of horse serum, at intervals of one or two weeks, is more likely to increase the hazard of a later injection of serum than is, for example, a single prophylactic dose of diphtheria antitoxin.

2. The sensitized guinea-pig can be protected from fatal anaphylaxis by the injection of a very minute dose of the specific protein. This produces very mild shock, from which the animal quickly recovers; and subsequently the animal is, for a time, incapable of the typical response to the injection of a large amount of the protein. In the treatment of sensitive patients attempts are made to utilize the same protective mechanism, the method of desensitization being an effort to produce this state of anti-anaphylaxis. Human behavior herein departs from the laboratory analogue in that the sensitive patient is not invariably protected from severe reaction by the administration of minute or graduated doses of serum. In fact, it is not certain that such a method ever protects. Nevertheless, good clinical practice supports such a procedure, even though it is not invariably successful; it is unquestionably advantageous to observe the effect of initial small doses of serum on the sensitive patient, whether or not they protect him against subsequent larger ones.

Precautions.—When serum is to be given, certain precautions are essential. These measures are particularly important if the intravenous route is to be employed.

History. A careful history regarding hypersensitiveness should be secured as a preliminary. Patients who are allergic to various substances, as indicated by attacks of asthma, hay fever, eczema, and urticaria should be regarded with suspicion. Inasmuch as horse serum is most commonly used, those who are sensitive to horse hair, horse dander, and horse serum, are the subject of gravest concern. These individuals, horse asthmatics, commonly develop asthmatic symptoms when in the vicinity of a horse and cannot ride upon or behind a horse in comfort; one such patient developed severe asthma from horse manure spread on the lawn outside his window. Most horse asthmatics are so extremely sensitive to all horse proteins that they cannot be given horse serum without extreme risk; but a few are so specifically sensitive to cutaneous emanations that serum does not produce a response.

A history of previous injections of (horse) serum is suggestive, although not necessarily productive of hypersensitiveness. Toxin-antitoxin is particularly apt to sensitize, but toxoid, which contains no serum, does not sensitize, and injections of vaccine are, of course, not significant.

Tests for Hypersensitiveness. In every case in which the history is suggestive, tests for hypersensitiveness should be conducted as a preliminary to treatment. It is not amiss to test every case if time permits.

The simplest test consists of the application of a drop of undiluted serum to a superficial scratch on the skin. In sensitive patients a definite reaction usually appears in less than thirty minutes, in the form of an urticarial wheal surrounded by a zone of erythema. The size and promptness of appearance of a reaction is roughly parallel to

the degree of sensitization. A few individuals are generally hypersensitive but lack skin sensitization, so that the absence of a skin reaction is not absolute evidence of safety; a positive skin reaction, however, is a significant warning.

The intracutaneous test is a more refined method, which at the same time introduces some risk of a general reaction. This consists of the intradermal injection of one-tenth cubic centimeter of a one to one hundred dilution of serum in normal saline. A positive reaction appears in from ten to forty minutes, and is similar to the foregoing.

The ophthalmic test consists in applying upon the conjunctiva a drop of diluted or undiluted serum. A reaction consisting of reddening and injection of the conjunctiva appears in a few minutes. When this reaction has definitely appeared, it should be promptly neutralized by the instillation of one to one thousand epinephrin solution, lest ulceration of the conjunctiva be produced.

Desensitization. In all cases in which history or tests indicate the possibility of reactions, the first dose of serum should be very minute, succeeding doses may be given at intervals in increasing amounts, while observing the local and systemic effects of previous doses. This is, of course, an effort to apply the phenomenon of anti-anaphylaxis to clinical use. Many good observers feel that desensitization is a futile gesture, which confers no real protection and is directed against an accident which seldom occurs; nevertheless, it affords a certain degree of safety, and at least permits the clinician to observe the results of minute doses before undertaking the injection of larger amounts.

Desensitizing injections should be made subcutaneously, or subcuticularly, *in an extremity* in such a location that if a generalized reaction occurs a tourniquet may be applied proximal to the site of injection so as to impede absorption. As far as possible all injections of serum should be in a similar location, so that if the necessity arises absorption may be caused to proceed slowly.

The amount of serum first administered should be based on the history and the skin reaction. In very sensitive cases one-half cubic centimeter of a one to one thousand dilution is given, less sensitive cases receiving a one to one hundred or one to ten dilution. Subsequent doses, and the interval between doses, may be decided upon by the response to previous injections. Commonly, injections may be repeated every thirty to forty minutes, using one-half cubic centimeter of 1 to 1000, 1 to 100, 1 to 10, and undiluted serum, following this with the entire dose intramuscularly.

Administration. The intramuscular route meets most requirements for therapy and should usually be employed. The subcutaneous route permits slower absorption and should be reserved for prophylactic serum. The intravenous route is most dangerous, and reactions from its use are most difficult to control. It should be used only for more serious illnesses, which call for serum therapy as an emergency measure, and should very rarely be employed if there is significant evidence of hypersensitiveness. If in the serum-sensitive patient the need for intravenous therapy seems definite, the above desensitizing procedures should be carried out, and then serum given intravenously in similar amounts and in similarly graduated dilutions.

Dextrose solution injections are an important adjuvant to serum therapy. Not only do these reduce protein reactions, but they help to prevent anaphylaxis-like reactions. When serum is to be given intravenously the dextrose solution may first be started, small desensitizing amounts of serum injected along with the dextrose, and finally the flow of the dextrose interrupted by the introduction of serum, which is, in turn, followed by more dextrose.

Treatment of Shock. Serum must never be given in any manner without having epinephrin solution at hand for instant injection. If signs of anaphylaxis-like shock appear, further absorption should be impeded, if the site is accessible, by a tourniquet, and the patient given epinephrin (1 to 1000) in physiological amounts—enough to cause blanching of the lips and acceleration of the pulse. Injections of epinephrin may be repeated; but dangerous symptoms are a matter of a very few minutes and must be promptly combated.

Morphin and other opiates are sometimes advisable in the treatment of prolonged reactions.

Delayed Reactions.—At intervals of three to ten or more days after serum injection, delayed reactions appear which are somewhat similar to immediate reactions, but are spread over a longer period of time and are much less violent or dangerous. The chief symptoms consist of urticaria, which may be most intolerably profuse and persistent; joint swellings, angioneurotic edema, enlargement of the lymphatic glands, and a variety of rashes of a general urticarial nature.

The reactions are caused to appear earlier after injection, and to be more violent, as a result of the factors which favor immediate reactions. A satisfactory clinical explanation of these symptoms is that they appear as a result of serum sensitivity that develops after, and as a result of the injection of serum. When this augments an existing slight degree of sensitivity, the resultant symptoms are caused to appear earlier and more violently.

The symptoms which appear at such an interval are rarely dangerous, but expose the patient to extreme discomfort. The injection of epinephrin will relieve symptoms, but after a short while they usually recur. Small injections of this drug may be given frequently or injections may be given at wider intervals; and as symptoms recur between injections, the site of the last injection may be gently massaged with resultant liberation of small amounts of epinephrin from the site of injection into the circulation. Ephedrin by mouth produces little relief.

Nursing care is of great value, and constant attention should be directed toward the patient's comfort. The frequent application to the superficial skin lesions of a variety of remedies affords relief. For this purpose calamin lotion may be used with the addition of menthol, alcohol, or phenol (phenol must be used with care, for extensive applications, in children); witch-hazel, alone or in combination with bicarbonate of soda; cooling baths with the addition of magnesium sulphate or bicarbonate of soda; iced compresses of solutions of boric acid, soda, or magnesium sulphate, or the application of ointments containing minute amounts of the synthetic local anesthetics.

The attendant itching, pain, irritability and restlessness of these patients is very difficult to relieve, and symptoms may be prolonged over many days. Sedatives, hypnotics, or opiates need to be freely used, as the patient's discomfort is altogether disproportionate to the lack of real severity.

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TREATMENT OF ACCIDENTS INCIDENT TO SERUM THERAPY

CLIFFORD SWEET, M. D. (242 Moss Avenue, Oakland).—Accidents incident to serum therapy should, so far as is possible, be prevented. No patient should be given serum until he has been studied to determine whether or not he is hypersensitive to the serum that is to be given. A careful history should be taken to determine whether or not there have been allergic states in related members of the family, and especially whether or not the patient has previously had asthma, hay fever, urticaria, eczema or other allergic attacks. A negative allergic history should never be accepted as evidence that the serum may be safely given, nor should a positive history be considered a contraindication to its use. A positive history may well emphasize the need for caution, but a negative history should never allow any decrease in the thoroughness of the preliminary study. A previous injection of horse serum, especially since so many children have had diphtheria toxin-antitoxin, and prophylactic tetanus antitoxin should be noted as having possibly established a state of hypersensitivity. The patient's reaction to the former injection of serum is of interest, but may not be accepted as indicating his present state of reactivity.

Every patient should be skin-tested with the serum to be used before it is injected. The few minutes required for this test will not delay needed treatment, and its use will decrease unpleasantly severe and at times fatal reactions to serum. If there is reason to believe that a severe state of hypersensitiveness exists, the scratch test with serum diluted one hundred to one thousand times with salt solution should be done. If this is negative, after twenty to thirty minutes 0.1 cubic centimeter of serum the same strength should be injected intra-, not subcutaneously. The injection of 0.1 cubic centimeter of dilute serum subcutaneously into a patient who is markedly hypersensitive may cause a severe or even fatal reaction. The idea that one may safely inject 1 cubic centimeter of undiluted serum subcutaneously as a test dose, and as a means of desensitizing the patient, is a dangerous one and should long since have passed out of practice. Intracutaneous injection should be done with the bevel of the hypodermic needle turned toward the surface of the skin in order to avoid the danger of unintentional subcutaneous injection.

If after an interval of fifteen or twenty minutes there are no urticarial pseudopodia about the site of the intracutaneous injection, 0.1 cubic centimeter of undiluted serum may be quite safely injected subcutaneously. Then if no symptoms develop, the entire dose may be injected subcutaneously, intramuscularly, or intravenously. If the injection is given intravenously, it should be given very slowly, and an additional factor of safety is added by diluting the serum with five to ten volumes of 5 to 10 per cent glucose solution, the mixture to be given slowly over a period in excess of fifteen minutes. However, if an urticarial wheal, especially one having pseudopodia about it, arises at the site of the intracutaneous test, the serum must then be given very cautiously in gradually increasing, divided doses over a period of four, five or six hours. For a patient who is evidently hypersensitive, one-tenth cubic centimeter of a 1 to 1000 dilution of the serum should be given subcutaneously. If a reaction of any moment occurs, it should be controlled with an injection of adrenalin, and after the lapse of twenty to thirty minutes the same dose of serum should be repeated. However, if the first subcutaneous injection (one-tenth cubic centimeter of serum diluted 1 to 1000) produces no reaction, a like amount (0.1 cubic centimeter) of serum diluted 1 to 100, 1 to 10, and undiluted, may be injected subcutaneously at intervals of twenty to thirty minutes. If no reaction is produced by the above injections, one-half and then one cubic centimeter may be injected during the next hour, followed by the remainder of the whole amount in divided doses during the next hour or two. However, if any of the doses on the above schedule produce a reaction of any severity, the same or a smaller dose should be used for the following injection, and increases made as gradually as may be necessary for the welfare of the patient, even though an entire day's time be required for the completion of the treatment.

Until one is certain that the patient is not dangerously hypersensitive to the serum, all subcutaneous or intramuscular injections should be made in an extremity so that absorption may be delayed by the application of a tourniquet proximal to the site of injection, should a reaction occur.

When giving serum, a fresh active solution of adrenalin should always be ready for immediate injection to relieve any symptoms that arise. Incidentally, if severe symptoms do arise, such as diffi-

culty in breathing, adrenalin should be given until relief is obtained. Often the failure to obtain relief from the injection of adrenalin is due to an inactive solution, but more often because an insufficient amount is injected. If the adrenalin solution is injected quickly, the greater part of it remains at the site of the injection, and is then released slowly by gentle massage or quickly by vigorous massage of the tissues which contain it. Pallor of the lips is the first dependable sign that an adrenalin effect has been obtained, and until this sign appears sufficient effect for relief of serious serum reaction has not yet occurred. The danger that one may give an overdose of adrenalin can be well guarded against by giving the injection in an extremity and then applying a snug tourniquet proximal to the site of the injection, whenever it is desirable to halt further absorption.

The patient who has been injected with serum should remain under close medical observation for at least one hour following the injection. Delayed reactions of serious grade are of sufficiently frequent occurrence to make this precaution imperative.

Serum Sickness. Patients should be warned that serum sickness may follow the injection of serum after the lapse of hours, or even as long as ten days. This warning should describe the fever, joint pains, and especially the outbreak of urticarial skin lesions that usually are its manifestations. By so warning his patient, the physician not only averts unfair criticism from himself, but also assists in educating the medical public concerning the whole matter of serum reaction, at the same time sparing his patient needless alarm.

The injection of adrenalin (1 to 1000 solution) is the only reliable means of giving direct relief to the patient suffering from serum sickness. The relief obtained from adrenalin is transient, but may be renewed from time to time over a period of twelve to eighteen hours by massage at the site of injection, provided a reasonably generous amount of adrenalin (0.5 to 1 cubic centimeter 1 to 1000 solution) has been injected. Relief from the intense itching of particularly troublesome areas of urticaria can be obtained by the local application of adrenalin to the affected area. Acetyl salicylic acid (aspirin) in adequate dose (0.3; [grains 5] at age six years) once in three or four hours should be given for relief of discomfort, while tub baths as hot as can be borne, to which liberal amounts of sodium bicarbonate have been added, usually allay the itching. Barbituric acid derivatives, such as phenobarbital, amytal, and sodium amytal, should be used to prevent disturbance during the sleeping hours. Treatment is of no avail except that the patient can be spared discomfort. Fortunately serum sickness is self-limited, and even though it may last several days, leaves no aftermath. Consequently, if the attending physician can persuade his patient that the benefit obtained, or the danger avoided is well worth the price of even a severe attack of serum sickness, all is well.

What Medical Care Costs the Average Family.—That the cost of medical care varies from zero in some families to more than the entire year's income in others is the general conclusion drawn from a survey of sickness costs among 36,000 Metropolitan Life Insurance Company employees and members of their immediate families. The highlights of this study are presented in summary form in the November issue of *The Modern Hospital* and the findings compared* with those of the Committee on the Costs of Medical Care (C. C. M. C.) which conducted a similar study of the annual costs of sickness among representative population groups.

Although records were received covering the costs of sickness for 120,334 persons, the survey cannot be said to cover 120,000 years of life. In the first place not all employees were in active service during the entire period in review and in the second place the study of family expense was limited to "natural"† families. Altogether there were 96,000 person-years of life exposed, of which approximately 34,000 were used in the study of costs for total families.

Since the employees live in the more thickly populated sections of the country the survey represents essentially an urban rather than a general population group. No returns from rural areas and few from towns of less than 5,000 were received.

The known incomes of the families were above those of the general population, 85 per cent of the annual incomes for the "natural" families falling into the $2,000 to $5,000 group.

Considering the proportion of families receiving certain types of medical care, the results of the Metropolitan and of the C. C. M. C. studies were remarkably similar. In both cases approximately 85 per cent of the families reported doctors' services, approximately 50 per cent dental service and 20 per cent hospital treatment. Among Metropolitan families, 89.1 per cent purchased drugs, 8.8 per cent paid for nurses' service and 21.5 per cent reported oculists' service. Among C. C. M. C. families, on the other hand, these percentages were 97.0, 17.3 and 13.4, respectively. This discrepancy may be explained by the difference in technic used in the two surveys.

Cost Varies Directly With Family Income.—That the cost of medical care varies directly with family income is confirmed by the Metropolitan and the C. C. M. C. findings. About 3.0 per cent of income was expended on medical care regardless of size of family, the per capita costs decreasing from $47.01 in families with no children to $13.44 in families with six or more children. In three-fourths of the cases of sickness studied individually, the expense per case was less in families with six or more children than in families with no children or with only one child.

The Most Frequent and Most Expensive Causes of Illness.—In both investigations it was found that the minor respiratory diseases and care of the teeth were the primary factors in sickness costs. Conditions responsible for the largest combined expense in order of importance were care of the teeth, puerperal conditions and minor respiratory conditions. The most expensive single illnesses were due to diseases of the bones, cancer, diseases of the lungs, hernia and intestinal obstruction, tumors, appendicitis, ulcers of the stomach and intestines, and goiter.

Costs of Hospitalized Illness.—The average expense of a case of hospitalized illness was $163. Actually, the illnesses varied in cost from less than $10 to more than $5,000 per case. In one-third of the cases the expense was greater than the average, in one-quarter greater than $200, and in almost one-fifth larger than $250 each.

In one-quarter of the cases hospitalized illnesses accounted for 90 per cent or more of the total family expense for medical care, in two-fifths for 80 per cent or more and in two-thirds for 50 per cent or more.

* Comparison is made between the Metropolitan crude results and the C. C. M. C. results adjusted for standard income and size of community distributions.

† A family consisting of husband and wife, or of father, mother and children, the head of which had been in continuous service with the Metropolitan for approximately two years.